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TITLE: Targeting Androgen Receptor in Breast Cancer: Enzalutamide as a Novel Breast Cancer Therapeutic

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14. ABSTRACT

Enzalutamide has clinical activity in breast cancer as a single agent and in combination with exemestane. Activity is seen in both triple negative AR+ BC and also ER+AR+ BC. Clinical data in Her2+ AR+ BC is too immature to make conclusions. The proposed clinical trials for Years 3-5 appear to be justified based on clinical activity and the current preclinical data.

15. SUBJECT TERMS

Breast cancer (BC) subtypes; androgen receptor (AR); preclinical modeling; enzalutamide; AR inhibition; resistance mechanisms; predictive biomarkers.

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Title: Targeting Androgen Receptor in Breast Cancer: Enzalutamide as a Novel Breast Cancer Therapeutic

Collaborating/Partnering PI: Anthony D Elias, MD

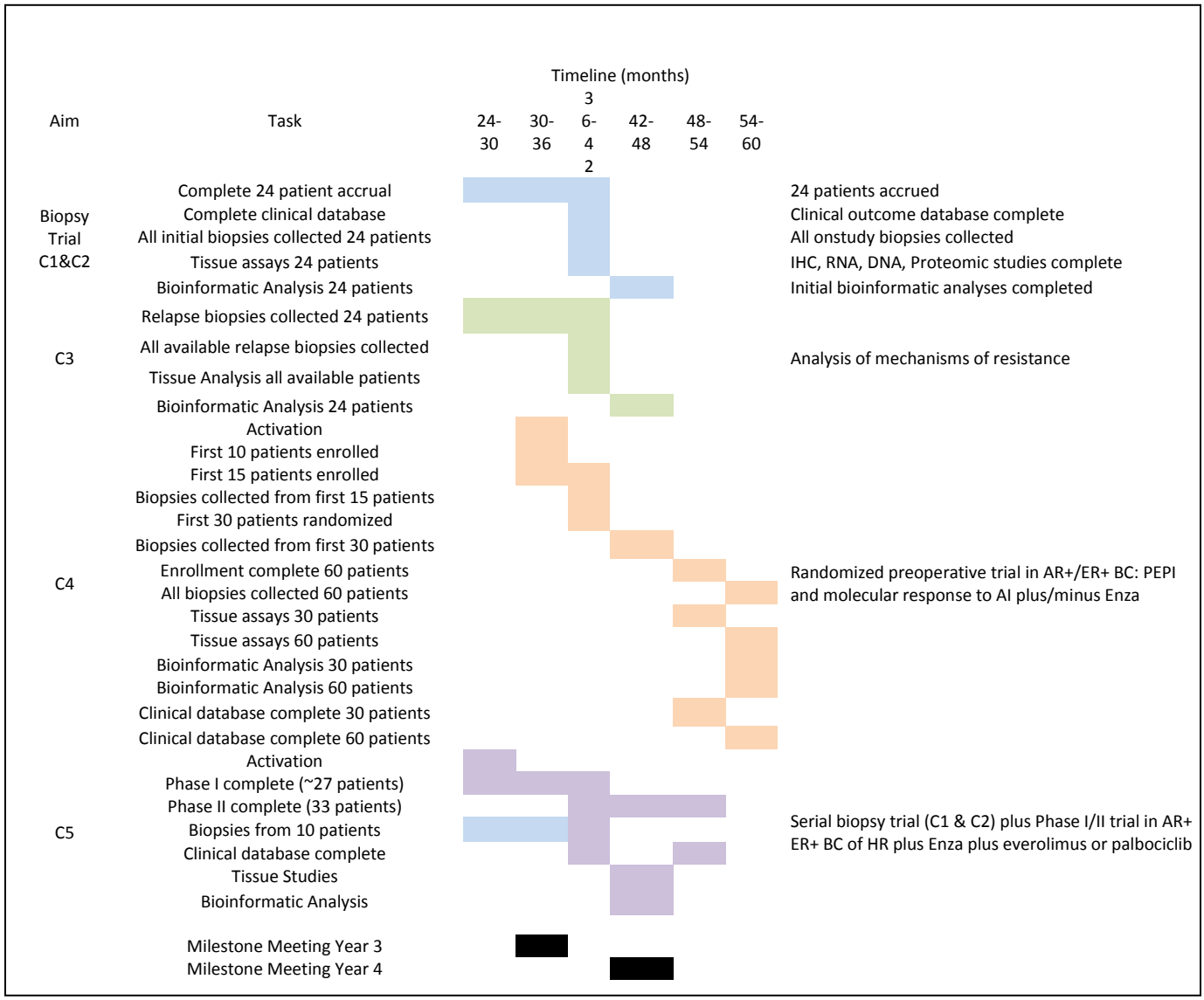
Contracting Organization: University of Colorado Anschutz Medical Campus

Report Date: 8/15/2015-8/14/2016

Type of Report: Third Annual Progress Report

Introduction

The central thesis of this grant is to understand the role of AR signaling in breast cancer subtypes, and understand how to best use an inhibitor of AR signaling, enzalutamide (enza), as a therapeutic agent in breast cancer. With the recognition that AR is expressed in all subtypes of breast cancer, that overexpression is frequently associated with relative resistance to therapy (both anti-estrogen and chemotherapy) (work of our



group and others), and with the advent of increasingly potent AR signaling inhibitors in prostate cancer, the area of anti-AR therapeutics in breast cancer is one of the most active worldwide. The preclinical portion of this grant serves to understand mechanism of action of AR signaling inhibition alone or in combination with other targeted agents in ER+, Her2+, or TNBC in preclinical models, and then perform biomarker analysis in human tissues obtained before, during and after treatment with enzalutamide. The clinical portion of this grant serves to obtain these tissues in concert with the overall clinical development of enzalutamide in the subtypes of breast cancer.

Keywords

Breast cancer (BC) subtypes; androgen receptor (AR); preclinical modeling; enzalutamide; AR inhibition; resistance mechanisms; predictive biomarkers; targeted therapy.

Overall Project Summary

Clinical Aim 1: To identify pretreatment molecular characteristics associated with lack of response and/or prolonged PFS (Patient Tissues).

Task 1: Serial Biopsy Trial (Elias, Traina, Schwartzberg, Petricoin, Patient advocates, Richer)

- The DOD sponsored serial biopsy trial titled "Exploratory Development of Predictive Biomarkers for Patients with Androgen-Receptor Positive (AR) Breast Cancer (BC) Treated with Enzalutamide (MDV3100); COMIRB 13-1473," is activated at the University of Colorado site and the West Clinic/University of Tennessee site.
- 6 patients with serial biopsies were enrolled.
    - Tissues have been processed by the UCCC Tissue Bank and distributed to the laboratories of Richer and Petricoin.
    - RPPA has been performed and has been analyzed
    - DNA mutational analysis has been performed.
    - RNA preparations made
    - IHC done for ER/AR/Ki67 and others in process.
    - Please see the Annual Report for Award Number W81XWH-13-1-0090 for all laboratory work done on the tissues and for all preclinical work.
- Accrual to this trial will not be completed due to the limitation that this biopsy trial was a companion to therapeutic trials of enzalutamide in breast cancer sponsored by Medivation and Astellas. Because those therapeutic trials were opened to large numbers of institutions that were not part of our DOD grant, and were completed very quickly, our accrual was limited. Current trials sponsored by those pharma partners are randomized double blind studies and are not suitable for serial biopsies as we cannot unblind the patients.
- On the other hand, the clinical development of enzalutamide was enhanced, making possible the forward-thinking investigator-sponsored trials as outlined for Years 3-5 in our grant.
- The new trials that are being developed in Clinical Aims 4 and 5 are suitable for serial biopsy, and will allow us to complete the Clinical Aims 1-3.

Task 2: Accrue 12 patients treated with enzalutamide onto serial biopsy trial (Elias, LoRusso, Traina, advocates) Year 0-Year 2 Month 7

- First 12 patients accrued completed (12) Month 7
- First 12 patients – clinical database complete Month 15
- All initial biopsies collected from 1st 12 patients Month 12

The new trials that are being developed in Clinical Aims 4 and 5 are suitable for serial biopsy, and will allow us to complete the Clinical Aims 1-3.

Task 3: Tissue assays and bioinformatics analysis (Richer, Thor, Jones, Elias, LoRusso, Traina, Petricoin, Gao)

- First 12 patients completed Month 18
- Bioinformatic analysis Month 24

The first 6 patients have completed tissue acquisition, assays have been performed and bioinformatic analysis is complete.

- Please see the Annual Report for Award Number W81XWH-13-1-0090 for all laboratory work done on the tissues and for all preclinical work.

Clinical Characteristics:

UPN	Age	Histology	ER arch	PR arch	Her2 arch	AR arch	Ki67 %	Adj CT	Adj HR	Prior CT	Prior HR	Regimen	Best Resp	TTP mos	OS mos	
001	78	IDC	3+ 96%	Pos	Neg	2-3+ 90%	20	No	Tam	4	7	E	PD	2	33+	
002	55	IDC	3+ 95%	3+ 63%	1+	2-3+ 80%	30	No	No	1	2	E	PD	2	14	
003	67	IDC	3+ 99%	?	Neg	2+ 80%	30	CAF	Tam	3	2	E	PD	2	5+	mut ESR1 Y537N
004	37	IMC/ IBC	Neg	Neg	Neg	1+ 30%	70	No	No	2	0	E	PD	2	3	
005	53	IDC	1+ 20%	Pos	Neg	2+ 90%	30	CMF	No	0	2	EF	SD	10	25+	mut ESR1 Y537S
006	57	ILC	3+ 95%	Neg	1+	3+ 60%	2	No	No	0	2	EF	SD	4	14	

- Heterogeneous patients with respect to ER status, prior treatment.
- ER/AR IHC from archived tissue (obtained from primary tumor) often dramatically different from the immediate pre treatment biopsy.
- Two patients with ER+ disease had mutated ESR1 in the pretreatment biopsy
- Using RPPA methodology to examine phosphoproteins, pre- vs post-enzalutamide tissues frequently demonstrated downregulation of various growth factor pathways.

Clinical Aim 2: To determine if a decrease in Ki67 or increase in apoptosis as measured by TUNEL in biopsies taken before treatment as compared to after 2-4 weeks of treatment or other to be determined genes or proteins are associated with lack of response and/or prolonged PFS.

Task 1: Accrue 24 patients treated with single agent enzalutamide (Elias, LoRusso, Traina, advocates)

- First half of patient accrual completed (12) Month 15
- First 12 patients – clinical database complete Month 15
- All 2-week biopsies collected from 1st 12 patients Month 15

Task 2: Tissue assays and bioinformatics analysis (Richer, Thor, Jones, Elias, LoRusso, Traina, Petricoin, Gao)

- 12 single agent patients Month 18
- Bioinformatic analysis completed Month 24

The first 6 patients have completed tissue acquisition, assays have been performed and bioinformatic analysis is complete.

- Please see the Annual Report for Award Number W81XWH-13-1-0090 for all laboratory work done on the tissues and for all preclinical work.

Clinical Aim 3: To determine if changes in molecular determinants between pre-treatment biopsies and tissue at time of disease progression can help identify resistance mechanisms.
Task 1: Accrue 24 patients treated with single agent enzalutamide (Elias, LoRusso, Traina, advocates)

- All relapse biopsies collected from 1st 12 patients Month 24

Three of the six patients with relapse have been biopsied at time of relapse.

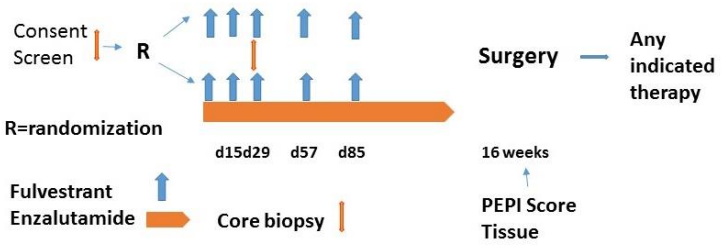
- Please see the Annual Report for Award Number W81XWH-13-1-0090 for all laboratory work done on the tissues and for all preclinical work.
- Rather than focus on a heterogeneous mix of breast cancer subtypes, we have chosen to focus on ER+/Her2- BC for clinical correlation. Astellas has chosen to develop enzalutamide (with chemotherapy) in TNBC. We have designed the trial outlined in Clinical Aim 5 to serve as the basis for these studies. This trial treats patients with metastatic ER+/Her2- breast cancer with fulvestrant plus enzalutamide. It is expected that over 90% of these patients will have tumors positive for AR expression. Fresh biopsies are obtained pretreatment, at 4 weeks on treatment, and at time of progression (optional).

Clinical Aim 4: To determine if enza can overcome *de novo* resistance to exemestane in postmenopausal women with T2 or larger ER+ BC treated preoperatively.
Task 1: Trial II: Randomized Preoperative trial in AR+/ER+ BC (Elias, LoRusso, Traina, advocates, Richer)

- Written protocol completed Month 21
- Submitted to Scientific Review Committee Month 21
- Submitted to IRBs (all institutions) Month 22
- DoD Human Research Protection Office (HRPO) Month 24

The Clinical Aim 4 trial was originally a randomized phase II trial of exemestane +/- enzalutamide given preoperatively for women with T2 or larger AR+/ER+ BC. This LOI was submitted to Astellas/Medivation in August 2015. Unfortunately, before it was evaluated, Astellas shut down their IIT program pending an internal assessment of their development plans for enzalutamide in breast cancer. This LOI was ultimately evaluated and rejected in 12/2015. An LOI for the same trial using fulvestrant +/- enzalutamide was submitted in 1/2016 and accepted by Astellas in 2/2016. The full protocol was written and submitted to Astellas and to the UCCC Scientific Review Committee in May 2016. Because >90% of ER+ BC is also AR+, AR IHC is not being used to select patients. It was approved, then submitted for an FDA IND application in 8/2016. It has been declared IND exempt by CTEP. It is now submitted to our IRB (COMIRB 16-1042). Once IRB approval has been obtained, it will be submitted to HRPO and to the IRBs at MSKCC and University of Tennessee prior to activation.

Preoperative Fulvestrant +/- Enzalutamide
Eligibility: >=T2; ER+/Her2-



If pre- or perimenopausal, goserelin 3.6 mg sq every 4 weeks (or equivalent)
Samples to be collected:

- Tumor tissue: at baseline, at 4 weeks, at time of surgery (16 weeks)
- Plasma: at baseline, at 4 weeks, at time of surgery (16 weeks)

- We completed a phase I pharmacokinetic trial combining enza with fulvestrant and will be reported results at SABCS 2015 (Elias et al). Findings demonstrated safety of full doses of each agent, and no evidence for PK interaction between the two agents. Manuscript is in preparation.
- **Elias AD**, Burris HA, Patel MR, Schwartzberg LS, **Richer JK**, Kavalerchik E, Stopatschinskaja S, Gibbons J, Markova D, Steinberg JL, Traina TA. MDV3100-08: a phase I study evaluating the safety and pharmacokinetics of enzalutamide plus fulvestrant in women with advanced hormone receptor-positive breast cancer. Proc SABCS 2015, accepted poster presentation; manuscript in preparation.

Primary endpoint: To evaluate whether the addition of enzalutamide to fulvestrant treatment for ~4 months in women with ≥T2 ER+/Her2- BC will achieve a PEPI score of 0 at time of surgery in 32%. PEPI (preoperative endocrine prognostic index) is a model that combines ER, pathologic tumor site, nodal status, and Ki67 score at time of surgery to predict subsequent risk of recurrence. PEPI = 0 means ypT < 1cm; Ki67 <10%; N0; ER+. PEPI is used to guide postoperative therapy in a number of neoadjuvant breast cancer trials (NCT01723774, NCT02236572, NCT01923168, NCT01953588). Fulvestrant has been shown to be more active against ER+ MBC than AIs in the randomized phase II FIRST trial. Phase III confirmation of fulvestrant vs. AI in MBC in the FALCON trial (NCT01602380). The ALTERNATE trial, accruing in NCTN, randomizes women with cT2-4 N0-3 M0 ER+/Her- breast cancer to anastrozole, fulvestrant, or the combination for 6 months prior to surgery (NCT01953588).

Statistical design: From the literature, preoperative aromatase inhibitor (AI) achieved PEPI score of 0 in 16%. We expect to achieve PEPI score of 0 in 32% for fulvestrant plus enzalutamide. Fulvestrant alone would likely be intermediate. We are using a Simon 2-stage design for the combination (experimental) arm: if ≤ 3 PEPI = 0 in first 22 evaluable patients, then will terminate entire trial. If ≥ 4 achieve PEPI = 0, then will increase arm size to 34. The probability of early termination is 0.52. We will have an 80% power with a type I error rate of 0.08. The trial has a concurrent control arm of fulvestrant alone with 27 patients. If the true PEPI = 0 is >16%, the observable rate has a 90% likelihood of being > 6%. We anticipate ~10% inadequate tissue specimens. A total of 49-61 patients will be randomized and treated.

Grant Hypotheses (from serial tissue biopsies):

- Decrease in Ki67 after ~4 weeks of treatment to below 10% will be associated with response to therapy and will correlate with improved PEPI scores.
- Certain pretreatment molecular characteristics (such as AR:ER ratio in ER+ tumors, Her2 status, PI3K pathway mutations, or others) will be associated with lesser response and poorer PEPI score.
- High AR expression will be associated with resistance to anti-estrogen therapy. Its blockade may enhance response.

Eligibility: At least 18 years of age, ER+/Her2- BC (>90% will be AR+), stage ≥cT2, planned to get local surgery,

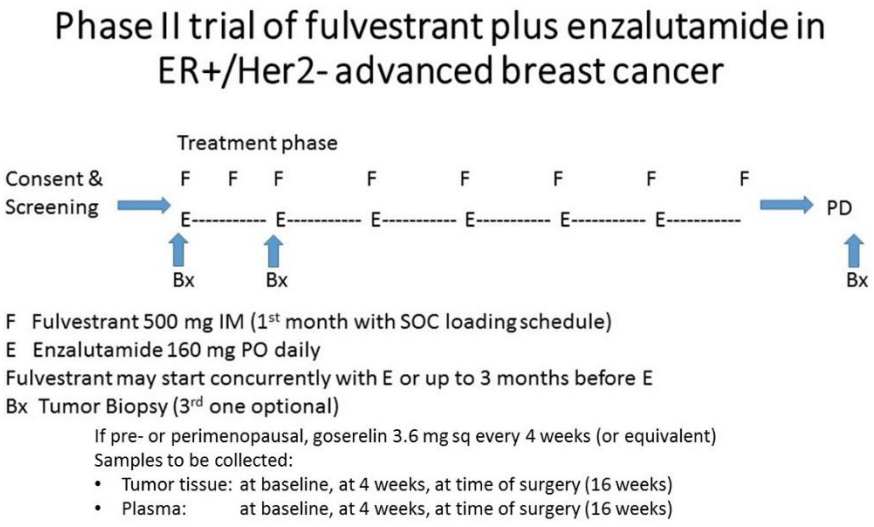
PS 0-2, safe to biopsy, no prior treatment. Women must be postmenopausal, or if pre- or peri-menopausal, will require concurrent ovarian suppression.

Clinical Aim 5: To determine the maximum tolerated dose and toxicity of enza when combined with the most promising combinations as defined in the preclinical modeling experiments during Years 1-2. As an example, a combination of enza with everolimus +/- a chemotherapy agent in previously treated metastatic TNBC.

Task 1: Trial III: Phase I/II trial in AR+/TN BC: Enzalutamide plus everolimus (Traina, Elias, LoRusso, advocates, Richer)

- Written protocol completed Month 21
- Submitted to Scientific Review Committee Month 21
- Submitted to IRBs (all institutions) Month 22
- DoD Human Research Protection Office (HRPO) Month 24

Support for this trial was not granted by Medivation and Astellas. An alternative trial, as presented at the Milestone Meeting in May 2015, was a Phase I/II trial in AR+ ER+ BC: Enzalutamide plus exemestane or fulvestrant with the addition of either everolimus or palbociclib. This LOI was submitted to Medivation and Astellas and was rejected for support or drug supply. Ultimately, once the phase I of fulvestrant plus enzalutamide was completed and reported, the following phase II trial was approved, then submitted for an FDA IND application in 8/2016. It has been declared IND exempt by CTEP. It has been submitted to our IRB (COMIRB 16-1001). Once IRB approval has been obtained, it will be submitted to HRPO and to the IRBs at MSKCC and University of Tennessee prior to activation.



Primary Endpoints: To determine the clinical benefit rate (CBR) of adding enzalutamide to fulvestrant treatment in women with ER+/Her2- advanced BC. To evaluate the safety and tolerability of fulvestrant plus enzalutamide. *Statistical Design:* Open label single arm phase II trial with 24 patients. Undesirable clinical benefit rate (CBR at 24 weeks) would be ≤10%. Desirable CBR would be ≥30%. This would provide 89% power with a one-sided ? of 0.085. If ≥5/24 patients have CBR of ≥24 weeks, then combination warrants further evaluation. We anticipate 10% inadequate tissue specimens.

Grant Hypotheses (from serial tissue biopsies):

- Decrease in Ki67 after ~4 weeks of treatment to below 10% will be associated with response to therapy and will correlate with CBR.
- Pretreatment molecular characteristics (such as AR:ER ratio in ER+ tumors, Her2 status, PI3K pathway mutations, or others) will be associated with CBR.
- High AR expression will be associated with resistance to anti-estrogen therapy. Its blockade may enhance response.

- Tissue at time of disease progression will be enriched for genes/proteins/mutations representing resistance mechanisms

Eligibility: At least 18 years of age, ER+/Her2- BC (>90% will be AR+), metastatic, tumor tissue available and safe for serial biopsy, candidate for fulvestrant therapy, PS 0-2, safe to biopsy, no CNS disease. Women must be postmenopausal, or if pre- or peri-menopausal, will require concurrent ovarian suppression.

Key Research Accomplishments:

Enzalutamide has clinical activity in breast cancer as a single agent and in combination with endocrine therapies.

Tissues from 6 patients have been processed, RPPA, IHC and DNA mutation analysis has been completed. Bioinformatic analysis underway.

Two clinical trials have been submitted to our local IRB (COMIRB 16-1042 and COMIRB 16-1001) to complete the clinical aims of this grant. We should be able to submit these to HRPO by October 2016.

Please see the Annual Report for Award Number W81XWH-13-1-0090 for all laboratory work done on the tissues and for all preclinical work.

Conclusion:

Enzalutamide has clinical activity in breast cancer as a single agent and in combination with exemestane. Activity is seen in both triple negative AR+ BC and also ER+AR+ BC. Clinical data in Her2+ AR+ BC is too immature to make conclusions. The proposed clinical trials for Years 3-5 appear to be justified based on clinical activity and the current preclinical data.

Publications, Abstracts, and Presentations:

Papers:
Dawn R. Cochrane, Sebastian Bernales, Britta M. Jacobsen, Diana M. Cittelly, Erin N. Howe, Nicholas C. D'Amato, Nicole S. Spoelstra, Annie Jean, Paul Jedlicka, Kathleen C. Torkko, Andy Protter, Anthony D. Elias and J. K. Richer. Role of the Androgen Receptor in Breast Cancer and Preclinical Analysis of Enzalutamide. BREAST CANCER RESEARCH 2014 Jan 22;16(1). PMID: 24451109

Designated as Highly Cited by the journal Breast Cancer Research.

Barton VN, D'Amato NC, Gordon MA, Lind HT, Spoelstra NS, Babbs B, Heinz RE, Elias AD, Jedlicka P, Jacobsen BM, Richer JK. Multiple molecular subtypes of triple negative breast cancer depend on androgen receptor for proliferation and invasion. Molecular Cancer Therapeutics 2015; 14: 769-778. PMID: 25713333

Barton VN, Gordon MA, Christenson JL, D'Amato NC, Elias A, Richer JK. Androgen receptor biology in triple negative breast cancer: a case for AR+ and quadruple negative disease subtypes. Horm Cancer 2015 Jul 23, epub ahead of print. PMID: 26201402.

Abstracts:

Elias AD, Burris HA, Patel MR, Schwartzberg LS, **Richer JK**, Kavalerchik E, Stopatschinskaja S, Gibbons J, Markova D, Steinberg JL, Traina TA. MDV3100-08: a phase I study evaluating the safety and pharmacokinetics of enzalutamide plus fulvestrant in women with advanced hormone receptor-positive breast cancer. Proc SABCS 2015, accepted poster presentation; manuscript in preparation.

Dr. Elias gave the following presentation:
Elias A. What is the androgen receptor doing in breast cancer and can we target it? 14th Annual International Congress on the Future of Breast Cancer. PER. Huntington Beach, CA 7/17/15.

Inventions, Patents and Licenses: Nothing to report

Reportable Outcomes: Nothing to report.
Please see the Annual Report for Award Number W81XWH-13-1-0090 for all laboratory work done on the tissues and for all preclinical work.

Other Achievements: Please see publication/abstract list.

Traina TA, Yardley, DA, Patel M, Schwartzberg L, Elias A, Gucalp A, Peterson AC, Hannah A, Gibbons J, Khondker Z, Hudis CA, LoRusso P. A phase 1 open-label, dose-escalation study evaluating the safety, tolerability, and pharmacokinetics of enzalutamide (previously MDV3100) alone or in combination with an aromatase inhibitor in women with advanced breast cancer. SABCS 2013 PD3-6 (A938), accepted, poster discussion. This demonstrated that the PK and single agent toxicity of enzalutamide in female breast cancer patients was the same as that of male prostate cancer patients.

Traina TA, Yardley DA, Patel MR, Schwartzberg LS, Elias A, Gucalp A, Blaney ME, Gibbons J, Hudis CA, LoRusso P. A phase 1 open-label study evaluating the safety, tolerability, and pharmacokinetics of enzalutamide alone or combined with an aromatase inhibitor in women with advanced breast cancer. IMPAKT 2014 Breast Cancer Conference May 2014, Abstract 214. This demonstrated that enzalutamide caused an 80% drop in AUC of anastrozole and a 50% drop in the AUC of exemestane via CYP3A4 induction. No new safety signals were observed.

Schwartzberg LS, Yardley DA, Elias A, Patel MR, Gucalp A, Burris HA, Peterson AC, Hannah AL, Blaney ME, Gibbons J, Tudor IC, Steinberg JL, LoRusso P, Infante JR, Hudis CA, Traina TA. Enzalutamide plus exemestane: a pilot study to assess safety, pharmacokinetics, and effects on circulating estrogens in women with advanced hormone-positive breast cancer. Proc ASCO 2014. This demonstrated that enzalutamide plus double dose exemestane resulted in equivalent PK and maintenance of estradiol suppression as single agent standard dose exemestane. No new safety signals were observed. Therefore for ongoing trials, double dose exemestane (eg, 50 mg daily) will be used.

Elias AD, Burris HA, Patel MR, Schwartzberg LS, Richer JK, Kavalerchik E, Stopatschinskaja S, Gibbons J, Markova D, Steinberg JL, Traina TA. MDV3100-08: a phase I study evaluating the safety and pharmacokinetics of enzalutamide plus fulvestrant in women with advanced hormone receptor-positive breast cancer. Proc SABCS 2015, accepted poster presentation. This demonstrated that there was no significant PK interaction between fulvestrant and enzalutamide. No new safety signals were observed.

Please see the Annual Report for Award Number W81XWH-13-1-0090 for all laboratory work done on the tissues and for all preclinical work.

References:

Papers:
Dawn R. Cochrane, Sebastian Bernales, Britta M. Jacobsen, Diana M. Cittelly, Erin N. Howe, Nicholas C. D'Amato, Nicole S. Spoelstra, Annie Jean, Paul Jedlicka, Kathleen C. Torkko, Andy Protter, Anthony D. Elias and J. K. Richer. Role of the Androgen Receptor in Breast Cancer and Preclinical Analysis of Enzalutamide. BREAST CANCER RESEARCH 2014 Jan 22;16(1). PMID: 24451109

Designated as Highly Cited by the journal Breast Cancer Research.
Barton VN, D'Amato NC, Gordon MA, Lind HT, Spoelstra NS, Babbs B, Heinz RE, Elias AD, Jedlicka P, Jacobsen BM, Richer JK. Multiple molecular subtypes of triple negative breast cancer critically rely on androgen receptor and respond to Enzalutamide in vivo. Molecular Cancer Therapeutics 2015; 14: 769-778. PMID: 25713333

Abstracts:
D'Amato, NC, D Cochrane, N Spoelstra, A Chitrakar, B Babbs, A Protter, AD Elias, and J Richer. (Mar 2014) Inhibiting Androgen Receptor Nuclear Localization Decreases ER Activity and Tumor Growth in ER+ Breast Cancer. University of Colorado Postdoctoral Research Day, Aurora, CO. * won best overall poster award.

Barton VN, D'Amato N, Gordon M, Elias, A, and JK Richer. Targeting androgen receptor decreases proliferation and invasion in preclinical models of triple negative breast cancer. Presented at University of Colorado Cancer Center Annual Retreat "Novel Experimental Models for Cancer Research," September 2014. * Won outstanding poster award.
Elias A, Richer JK, LoRusso P, Peterson AC, Steinberg J, Mordenti J, Lopez C, Hudis C, Traina T. MDV3100-08: A phase 1 open-label, dose-escalation study evaluating the safety, tolerability, and pharmacokinetics of MDV3100 in women with incurable breast cancer. ASCO 2012, TPS668.

Traina TA, Yardley, DA, Patel M, Schwartzberg L, Elias A, Gucalp A, Peterson AC, Hannah A, Gibbons J, Khondker Z, Hudis CA, LoRusso P. A phase 1 open-label, dose-escalation study evaluating the safety, tolerability, and pharmacokinetics of enzalutamide (previously MDV3100) alone or in combination with an aromatase inhibitor in women with advanced breast cancer. SABCS 2013 PD3-6 (A938), accepted, poster discussion.

Traina TA, Yardley, DA, Patel M, Schwartzberg L, Elias A, Gucalp A, Peterson AC, Hannah A, Gibbons J, Khondker Z, Hudis CA, LoRusso P. A phase 1 open-label, dose-escalation study evaluating the safety, tolerability, and pharmacokinetics of enzalutamide (previously MDV3100) alone or in combination with an aromatase inhibitor in women with advanced breast cancer. SABCS 2013 PD3-6 (A938), accepted, poster discussion.

Traina TA, Yardley DA, Patel MR, Schwartzberg LS, Elias A, Gucalp A, Blaney ME, Gibbons J, Hudis CA, LoRusso P. A phase 1 open-label study evaluating the safety, tolerability, and pharmacokinetics of enzalutamide alone

or combined with an aromatase inhibitor in women with advanced breast cancer. IMPAKT 2014 Breast Cancer Conference May 2014, Abstract 214.

Schwartzberg LS, Yardley DA, Elias A, Patel MR, Gucalp A, Burris HA, Peterson AC, Hannah AL, Blaney ME, Gibbons J, Tudor IC, Steinberg JL, LoRusso P, Infante JR, Hudis CA, Traina TA. Enzalutamide plus exemestane: a pilot study to assess safety, pharmacokinetics, and effects on circulating estrogens in women with advanced hormone-positive breast cancer. Proc ASCO 2014.

Elias AD, Burris HA, Patel MR, Schwartzberg LS, Richer JK, Kavalerchik E, Stopatschinskaja S, Gibbons J, Markova D, Steinberg JL, Traina TA. MDV3100-08: a phase I study evaluating the safety and pharmacokinetics of enzalutamide plus fulvestrant in women with advanced hormone receptor-positive breast cancer. Proc SABCS 2015, accepted poster presentation.

D'Amato NC, Jacobsen BM, Cochrane DR, Spoelstra NS, Babbs BL, Elias A, Richer JK. Inhibiting androgen receptor nuclear localization decreases estrogen receptor (ER) activity and tumor growth in ER+ breast cancer. Proc SABCS 2014, P3-04-06

Gordon MA, D'Amato N, Gu H, Wong D, Elias A, Richer JK. Targeting multiple pathways in breast cancer: Androgen receptor, HER2, and mTOR. Proc SABCS 2014, P6-03-07.

Gordon MA, D'Amato N, Gu H, Liu B, Elias A, Richer JK. The anti-androgen enzalutamide synergizes with trastuzumab and everolimus to inhibit breast cancer growth via distinct mechanisms. Endocrine Society 2015.

Website(s) or other Internet site(s)
List the URL for any Internet site(s) that disseminates the results of the research activities. A short description of each site should be provided. It is not necessary to include the publications already specified above in this section.

Expert Opinion piece in Oncology PracticeUpdate http://www.practiceupdate.com/journalscan/9370 or http://prac.co/j/5960d32c-988b-423e-ba24-14ca5c8cc39a?elsca1=soc_share-this acknowledgement of federal support –no

Highlight of Cochrane DR et al Breast Cancer Research 2014 in Feb issue of 2014 NATURE REVIEWS CLINICAL ONCOLOGY. acknowledgement of federal support –yes